REMARKS

Claims 70-82 are pending in this application. Claims 74-80 are withdrawn from consideration. Claims 81-82 have been added and their support can be found in the original application as filed on page 12. claims 1 and 2. Applicant believes the application is in condition for allowance and respectfully request they be entered and approved.

CLAIM REJECTIONS

Claims 70-73 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,502,077 to Breivik et al. ("Breivik"), U.S. Patent No. 5,604,216 to Horrobin ("Horrobin"), U.S. Patent No. 5,663,156 to Granja et al. ("Granja"), and U.S. Patent No. 3,031,376 to Levin et al. ("Levin") in view of Bundgaard ("Design of Prodrugs"). To the extent the rejections may be applied to the claims as amended, these rejections are respectfully traversed.

Claim 70 recites a composition for lowering LDL-cholesterol levels or elevating HDL-cholesterol levels in the blood of a mammal, comprising one or more esters of a carboxylic acid and a polycosanol, wherein the carboxylic acid is selected from the group consisting of eicosapentaenoic acid, docosahexaenoic acid, linoleic acid, arachidonic acid and linolenic acid and wherein the polycosanol is selected from the group consisting of docosanol, tetracosanol and hexacosanol.

The Examiner cites that Breivikl, Horrobin, Granja, and Levin teach providing ester forms of the recited carboxylic acids and ester forms of the recited alcohols for the stimulation of the heart and treatment of cardiovascular diseases and conditions. The references do no specifically teach that the ester forms are the ester of the recited carboxylic acid with the recited alcohol. The Examiner further states that one of ordinary skill in the art at the time the invention was made would have been motiviated to form an ester prodrug having the carboxylic acid and polycosanol moieties, with the expectation of providing a suitable means for delivery of the individual therapeutic agents for the treatment of cardiovascular disease and the treatment of the heart from the Bundgaard reference.

The Applicant has previously argued that Olestra is an example of an ester of a fatty acid that is not hydroysable in vivo and that it is not prima facie obvious that pancreatic esterases

would act on polycosanol esters with PUFA to hydrolyz the compound in vivo. The Examiner asserts that Olestra is an exception to the generally accepted mechanism of the action of the pancreatic lipases on fatty acid esters. However, waxes, either of the plant or animal type, are not digested by pancreatic lipases. Waxes are esters of policosanols and fatty acids. Patents for policosanol mixtures and their therapeutic uses include: US6,465,526; US6,235,795; US5,865,316; US6,663,156; and US5,952,393. These mixtures are obtained from waxes of different origin, such as sugarcane wax, rice bran wax or bee wax. Therapeutic effects are claimed exclusively for the free policosanols which were obtained from said waxes upon first saponifying these waxes. From the EFSA Journal (2004) 92,1-5:

"According to the literature, the oil content of the muscle meat of Oilfish and Escolar amounts to 18 - 21 % and the oil contains > 90 % wax esters. In these wax esters, C14 - C22 fatty acids are esterified with fatty alcohols of similar chain length. The wax esters will remain in the cooked fish if the preparation is not performed properly. Consuming 100 g of smoked Escolar or Oilfish would then lead to an exposure of about 20 g wax esters. As human lack the ability to digest wax esters, they will pass through the gastro-intestinal system. During the passage, they may cause diarrhoea and other acute gastro-intestinal symptoms when present in sufficient amounts. The symptoms can be dramatic but are seldom long lasting. Although the exact mechanism behind the effects is not fully understood, they are not considered to be caused by toxicity, as in the case of scombrotoxicosis, but rather by the lack of digestibility of these wax esters."

Since humans lack the ability to digest wax esters, it has been theorized that the policosanol esters of PUFA and other fatty acids are not hydrolized in vivo and there would have been no motivation to make synthetic wax esters. However, the Examples have shown that the policosanol esters of fatty acids have cholesterol loweing properties, not suggested by the prior art.

Further examples of esters which do not hydrolyze in vivo include: dialkyl dihexadecymalonate (DDM), trialkoxytricarballyate (TATCA); esterified propoxylated glycerol (EPG); and trialkoxycitrate (TAC). These "fat equivalents" are described in the web article from

Food Product design found at http://www.foodproductdesign.com/archive/1992/0492DE.html under the "Fat-based fat molecules" heading.

Yet another "exception" contrary to Bungaard's assertion is exhibited by beta-sitostanol and beta-sitostanol esters of fatty acids. Food composition containing beta-sitostanol for lowering cholesterol are disclosed in US Patent 5,932,562. US Patent 5,958,913 discloses food compositions for lowering cholesterol, containing esters of beta-sitostanol with common food fatty acids. But, surprisingly, said esters exhibited a significantly higher cholesterol lowering effect than beta-sitostanol alone, see US Patent 5,958,913, column 6, Table 3. Based upon the Examiner's theories, the Examiner would have expected the cleaving of the ester bond to regenerate the active beta-sitostanol. None of the fatty acids of rape seed oil are known for their cholesterol lowering effect. Whether sitostanol esters are hydrolyzed within the body or not, their unexpected effect with respect to free stanols arose from being administered in the form of an ester. This is what we claim for policosanol esters as well.

Thus, the Applicants have provided examples that olestra is not the exception to the rule for the "theory" of Bungaard. Furthermore, the applicants have provided examples of fatty acid esters of widely different chemical nature, whose cholesterol lowering effect do no fit in the "theory" of Bungaard as espoused by the Examiner.

No fees as a result of this response are required. However, the Commissioner is hereby authorized to charge any additional fees which may be required, or credit any overpayment, to Deposit Account No. 50-3420, reference 22106965-104181(VKF).

Respectfully submitted,

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